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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,823	10/24/2001	Merja Penttila	0933-0170P	1523
2292	7590	06/16/2004	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH			LIU, SAMUEL W	
PO BOX 747			ART UNIT	PAPER NUMBER
FALLS CHURCH, VA 22040-0747			1653	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,823	PENTTILA ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

status

- 1) ☒ Responsive to communication(s) filed on 6 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-24 is/are pending in the application.
- 4a) Of the above claim(s) 6-9, 16, 17 and 24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-5, 10-15 and 18-23 is/are rejected.
- 7) ☒ Claim(s) 1, 10 and 21-23 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>12/27/01&18/09/01</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of the claims

Claims 1 and 3-25 are pending.

Applicants' amendment filed 6 May 2004, which amends claims 1, 3, 5-6, 9-10, 20 and 23 and cancels claims 2, and applicants' request for extension of time of two months (filed 6 May 2004) have been entered.

Election/restriction

Applicants' election of Group I, claims 1, 3-5, 10-15 and 18-23 with traversal in the response filed 6 May 2004 is acknowledged. The traversal is on the ground(s) that Groups I-IV are linked by a special technical feature, i.e., specific characteristics of hydrophobin-like proteins which can be used to form amphipathic fusion protein easily separable in aqueous two-phase system (ATPS), and that Patent 5582520 does not teach or suggest the said technical feature (see pages 16-17). The applicants' argument has been fully considered.

The Patent 5582520 does not explicitly teach use of a *fusion protein* comprising hydrophobin or hydrophobin-like or parts thereof in ATPS-mediated separation of protein of interest. Yet, prior to the priority date of the instant application, Kohler, K. et al. (*Bio/tech.* (1991) 9, 642-646) teach a method of separating of proteins in ATPS comprising (i) preparing a fusion polypeptide comprising part of hydrophobin-like protein (i.e., tryptophan-rich oligopeptide), and (ii) subjecting said fusion protein to the ATPS-mediated protein separation. The Kohler et al. thus teach the technical feature of the instant claim 1. Note that claim 1 recites "...parts thereof"; this recitation has not been defined in the specification; thus, it is interpreted as any peptide or protein which behavior like hydrophobin, i.e., having high partitioning

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coefficient in hydrophobic phase of ATPS. Thus, the claimed invention does not constitute a special technical feature linking all claims, as defined by PCT Rule 13.2 and 37 CFR 1.475(a), as a single contribution over the art, and a holding of lack of unity is therefore proper.

Also applicants traverse the additional election requirement (see page 18, the 2nd paragraph). The Applicant's traversal has been under due consideration. The enzymes recited in claim 13 are examined in this Office action.

Thus, the pending claims 1, 3-5, 10-15 and 18-23 are examined in this Office action. Claims 6-9, 16-17 and 24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

IDS

The references of IDS filed 27 December 2001 and IDS filed 18 September 2001 have been considered.

Specification/Claim/ Objections

The disclosure is objected to because of the following informalities:

In page 13, line 13, line 13, "SDS-PAGE" should be spelled out in full for the first instance of use; see also page 10, line 29, "HFBI".

In claim 1, item a, "to a targeting protein" should be changed to "with a targeting protein"; and in item b, "ATPS separation" should be changed to "ATPS-mediated separation".

In claim 10, "cellbound" should be changed to "cell bound".

Claim 21 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only, i.e., cannot depend

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from any other multiple dependent claim, here it is claim 9. See MPEP § 608.01(n).

Accordingly, claim 21 has not been further treated on the merits.

In claim 22, “thermo separating polymer system” should be changed to “thermoseparating polymer system” in order to be consistent with the corresponding recitation in claim 20 from which claim 22 depends.

Claim 23 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only, i.e., cannot depend from any other multiple dependent claim, here it is claim 9. See MPEP § 608.01(n). Accordingly, claim 23 has not been further treated on the merits.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5, 10-15 and 18-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not describe a method of partitioning proteins in ATPS comprising preparing a fusion protein that comprises parts of hydrophobin-like protein polypeptides wherein “parts” has been neither defined nor described in the specification. Thus, without written

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description, one cannot know how to make and use the parts of hydrophobin-like protein. Thus, applicants are not in possession of the method using said parts of hydrophobin-like protein.

Also, the specification fails to describe derivatives of the aqueous two-phase system (claim 20).

Applicant has disclosed only the method of partitioning and separating proteins in ATPS comprising hydrophobin protein wherein the ATPS is PEG/salt, PEG/dextran and PEG/starch systems (see page 9-10) but not the derivative systems thereof. Therefore, the skilled artisan cannot envision (i) all the contemplated parts of hydrophobin-like possibilities recited in the instant claims, and (ii) the derivatives of ATPS. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

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Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1, 3-5, 10-15 and 18-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites “combining a protein to a targeting protein...”; the recitation is unclear as to whether or not said “combining” refers to recombinant fusion or non-covalent combination between the protein and targeting protein. Also, the claim recitation “...and parts thereof” (item *a*) is indefinite because the specification does not define what the parts of hydrophobin or hydrophobin-like protein is. See also claims 3-5, 11-12 and 24. In addition, claim 1, item *a*, recites the limitation “the phase”; there is no antecedent basis for this limitation in the

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claim. Further, the recitation “an ATPS separation” (item *b*) appears to be incomplete, suggest “an ATPS-mediated protein separation” because “separation” should follow the objective which is to be separated. The dependent claims are also rejected.

Claim 14 recites “a part thereof” is indefinite because the recitation is unclear as to whether or not the “part” refers to a fragment of the recited antibody, or a ligand that bind to the antibody protein.

The recitation of claim 19 “such proteins” (item *a*) and “such protein” (item *b*) render the claim indefinite because it is unclear whether such protein(s) refers to fusion protein(s) or the protein(s) of interest (a fusion partner) because claim 10 from which claim 9 depends recites the limitation “a protein of interest”.

Claim 20 recites “...or derivatives thereof”; the recitation is indefinite because the specification does not define what the derivatives of the claimed ATPS is.

Claim 21 recites the limitation “the detergent-based ATPS”; there is insufficient antecedent basis for this limitation in claim 20 from which claim 21 depends.

Claim 22 sets forth a Markush group; yet, the group contains only one element in the group. Because Markush group requires at least two members or components for constituting the group, claim 22 is indefinite.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless —

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Kohler, K. et al.

(*Bio/tech.* (1991) 9, 642-646).

Kohler et al. teach a method of separating of proteins in ATPS comprising (i) preparing a fusion polypeptide comprising part of hydrophobin-like protein (i.e., tryptophan-rich oligopeptide) and protein of interest, and (ii) subjecting said fusion protein to the ATPS-mediated protein separation. Since claim 1 language sets forth “hydrophobin-like proteins and parts thereof” wherein the “parts” of the “hydrophobin-like proteins, as written, would encompass any peptides or proteins which behavior like hydrophobin, i.e., having high partitioning coefficient in hydrophobic phase of ATPS. Thus, the Kohler et al. teaching anticipates the instant claim 1.

Claims 1 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Lang, K. et al. (US Pat. No. 5304310).

In Example 2, Lang et al. teach a method of separating of proteins in ATPS comprising (i) preparing a fusion protein (protein A-hirudin) comprising of hydrophobin-like protein (i.e., hirudin) and protein of interest, and (ii) subjecting said fusion protein to the ATPS-mediated protein separation. Note that the hirudin in said fusion protein behaviors like hydrophobin, i.e., partitioning in organic phase since Lang et al. teach that hirudin mediated partitioning in organic (hydrophobic) phase can be achieved via adjusting pH value before the addition of salt (see col. 3, lines 61-65). In view of the claim 1 language “hydrophobin-like proteins and parts thereof”,

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wherein the "parts" of the "hydrophobin-like proteins, as written, would encompass any peptides or proteins which behavior like hydrophobin having high partitioning coefficient in a hydrophobic phase of ATPS, the Kohler et al. teaching anticipates the instant claim 1.

Also, Lang et al. teach that in the above-mentioned method the protein of interest (i.e., protein A) is separated from an *E.coli* cell extract (see Example 2), as applied to claims 23.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.



Samuel Wei Liu, Ph.D.
Art Unit 1653, Examiner
May 25, 2004



ROBERT A. WAX
PRIMARY EXAMINER